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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/634,426	08/05/2003	Scott D. Kuduk	20851	8307

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MERCK AND CO INC
P O BOX 2000
RAHWAY, NJ 070650907

EXAMINER	
ROBINSON, BINTA M	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/634,426	KUDUK ET AL.	
	Examiner	Art Unit	
	Binta M. Robinson	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-37 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) 1-29 and 31 is/are allowed.

6)☒ Claim(s) 32-37 is/are rejected.

7)☒ Claim(s) 30 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Claims 1-37 are pending.

Claim 30 is objected to because the tables and the compounds are not separated from other compounds by commas or semi colons. This objection can be overcome if each compound and their respective table is separated from other compounds and tables by the phrase ";or".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32, 33, 34, 35, 36, and 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the treatment or prevention of pain or inflammation with the claimed compounds and the specification does not reasonably provide enablement for treating all types of cancer pain with bradykinin antagonists, and all of the diseases claimed in claim 3 with bradykinin antagonists. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

It is not established in the art to prevent pain or inflammation with any pharmaceutical drug.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The Nature of the Invention

The nature of the invention in claims 28-31 is the treatment of pain and inflammation, and the diseases stated in claim 36 with bradykinin antagonists.

The State of the Prior Art

The state of the prior art is that the Kallikrein-kinin system plays an important role in many physiological conditions such as homeostasis of circulation, inflammation, allergy, pain, shock, etc. Two types of kinin receptors are known, bradyking (BK) B1 and BK B2 receptor. B1 receptors are highly indicuible upon inflammatory stimiulation or tissue injury, suggesting that they are involved in inflammation and/or nociception and B2 receptors are constitutively expressed and mediate most physiological actions of kinins. No antagonists have been tested for the B1 receptor. (See Abstract of Hirayama et. al., Nippon Yakurigaku Zasshi). B2 antagonists have been shown to have some beneficial effects for rhinitis , asthma, systemic inflammatory response syndrome and sepsis and brain injury. The role of B1 receptors in the art is uncertain and is still being elucidated by the use of peptide type antagonists

or B1 receptor gene knockout mice. Further clinical evaluation of B1 antagonists is needed. (See See Abstract of Hirayama et. al., Nippon Yakurigaku Zasshi).

The predictability or lack thereof in the art

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of Bradykinin-mediated diseases, whether the bradykinin was promoted or inhibited would affect the possible treatment of any disease.

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by the compound of claim 1 and the inhibition of bradykinin, one of skill in the art is unable to fully predict possible results from the administration of the compound of claim 1 due to the unpredictability of the role of bradykinin, i.e. whether promotion or inhibition would be beneficial for the treatment of the diseases.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art

would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present

The specification is silent and fails to provide guidance as to whether the diseases listed as bradykinin-mediated diseases, require the antagonistic action against bradyknin or the promotion of bradykinin for treatment, i.e. the specification fails to provide a correlation between the diseases listed and the inhibition of bradykinin.

The presence or absence of working examples

There are not other working examples for any diseases listed in the specification. Also, the compounds which are discloses in the specification have no pharmacological data regarding the treatment of any other disease besides the rejection and have no data on the possible treatment of bradykinin-mediated diseases that require antagonistic action against bradykinin. Also, the specification fails to provide working examples as to how the listed diseases can be treated by the inhibition of bradykinin, i.e. again, there is no correlation between the diseases listed and inhibition of bradykinin.

The breadth of the claims

The breadth of the claims is that the compound of claim 1 can treat any pain, inflammation, and the diseases claimed in claim 36 with bradykinin antagonists.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what listed diseases would be benefited by antagonistic

action against bradykinin and would furthermore then have to determine whether the claimed compounds would provide treatment of the disease by the inhibiton of bradykinin.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the claim 1 for the treatment of an bradykinin-mediated disease. As a result necessitating one of skill to perform an exhaustive search for which bradykinin-mediated diseases can be treated by the compound of claim 1 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which bradykin-mediated diseases can be

treated by the compound encompassed in the instant claims, with no assurance of success.

Claims 1-29 and 31, are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)-272-1600.

BMR
June 11, 2004

JOSEPH K. McKANE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600